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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MCKELVEY, TERRY ALAN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,711	REBAR ET AL.	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2004 and 18 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28 and 30-52* is/are pending in the application.

4a) Of the above claim(s) *1,3,5,7-9,11-21,23,24,33-35,38 and 42-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,6,10,22,25-28,30-32,36,37 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/15/03; 2/5/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II (drawn to nucleic acid), species: DNA target sequence, zinc finger component comprising X(3)-Cys-X(2)-Cys-X(12)-His-X(3)-Z-X(4), target located in plant cell, further comprising an activation domain, claims 2, 4, 6, 10, 22, 25-28, 30-32, 36-37, and 39-41 in the reply filed on 8/3/04 and 11/18/04 is acknowledged. The traversal is on the ground(s) that follow.

1. The inventions must be both independent and distinct. This is not persuasive because this issue has long been settled. Concerning the applicants' interpretation of 35 U.S.C. § 121 that both independence and distinctness be present for restriction between two inventions to be proper, the law has long been established that dependent inventions may be properly divided if they are in fact "distinct" inventions. See M.P.E.P. § 802.01. The Courts have interpreted the statute to mean "or" instead of "and" in 35 U.S.C. § 121. Thus, there is no need to show or argue independence between the claimed inventions because the inventions are distinct, not independent.

2. Applicant argues that the Examiner has not demonstrated that the claims of Group I and II are distinct from each other

because proteins are not capable of self-replication and neither the claimed proteins nor the claimed polynucleotides can be purified from cells or organisms because they are non-naturally-occurring molecules, and the claimed proteins are too long (>60 amino acids) to be easily synthesized and purified using standard peptide synthesis techniques. This argument is not persuasive because the polynucleotides can be isolated from cells transformed with the polynucleotides (which cells are self-replicating), or isolated from self-replicating vectors such as plasmids, without producing or isolating the proteins and thus the production of the polynucleotides does not require the proteins. The proteins can be produced without requiring the polynucleotides because even if the proteins are not easily synthesized because of their length, they can be synthesized and thus they do not require the polynucleotides for their production. As evidence of this, synthesis of polypeptides in excess of 100 amino acids are taught throughout Canne et al (US Patent No. 6,326,468 B1), Example 5 for example. Another method which is specifically used in making sequence-specific binding proteins that recognize long sequences (16 base pairs in the example) is protein stitchery, such as that taught by Park et al ten years ago.

3. Applicant argues that they are not aware of any methods in which the claimed proteins can be used to isolate or label DNA and request that the Office provide examples of the asserted methods. This argument is not persuasive in overcoming the restriction because these uses of DNA binding proteins are extremely well known. For example, as taught in Pomerantz et al (US Patent No. 6,326,166 B1), "In one application, the chimeric proteins bind a selected nucleic acid sequence within a DNA or RNA and, as a result, mark or flag the selected DNA or RNA sequence, which can be identified and/or isolated from the DNA using known methods." (column 3, lines 38-42). The chimeric proteins in the reference are in the same class of proteins, sequence-specific binding proteins (most of which) comprise one or more zinc fingers like the claimed proteins.

4. Applicant argues that as amended the polynucleotides of Group II are now used in the methods of Group III and thus the restriction between Groups II and III should be withdrawn. This argument is not persuasive because now the following showing of distinctness applies:

Inventions of Group II and Group III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another

materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process, overexpression of the protein encoded by the polynucleotides, for use in preparing the isolated protein which is then used as taught by the specification.

5. Applicants also argue that it would not be unduly burdensome to search the inventions together because a search for any references relevant to one Group will reveal art relevant to the others (and would even save the Office time and resources). This argument is not persuasive because "revealing art relevant to the other groups" does not constitute a complete search which is required if those different inventions are searched and examined together. The different groups are each classified in class/subclasses from each other which is prima facie evidence of search burden to search together. Additionally, each group requires a different non-patent literature search because references that teach the protein do not necessarily teach the polynucleotide encoding the protein, and certainly do not necessarily teach the use of the polynucleotide in the claimed method. The same is true for the polynucleotide because references in this art often do not use

the polynucleotide in regulating expression of gene and often the protein encoded by the polynucleotide is not isolated. This is shown by the references cited below, some of which do not teach all three inventions. Therefore it would constitute an undue burden to search and examine the three groups together. It would not save the time of the examiner to search them together because time for the search and examination of an application is allotted based upon one independent or distinct invention per case. Spreading the time given for the instant case between three inventions necessarily results in a significant reduction of time per invention as compared to using all of the allotted time for the proper search and examination of one invention. The number of pending applications and reduction thereof has nothing to do with the appropriateness of the instant restriction requirement and thus is not persuasive in overcoming the restriction requirement.

6. Applicant argues that the Examiner has not indicated what the species are considered to be and on what basis they are distinct and thus Applicants traverse on the grounds that the election of species requirement is not adequately set forth. It is also argued that a search for any polynucleotide encoding an non-canonical zinc fingers that recognizes any target sequence and/or further encodes any functional domain and modulates

expression in any cell type would necessarily reveal relevant art to each of the alleged distinct species and therefore it would not be burdensome to examine the claim as a whole. This argument is not persuasive for the following reasons. First, obviously the applicant was able to understand the election of species requirement because the applicant successfully elected one from each species type between the two restriction/election responses. It is the claim structure that makes it difficult to describe and set forth the election of species because as claimed the application sets forth five different species types. Second, the distinctness comes from the fact that each species from each species type imparts a different structure on all or part of the claimed and elected polynucleotides. Each different protein structure is related by structure because the generic structure drawn to the basic non-canonical structure is present in each species, but they are distinct from each other because of the different specific structures that result the claimed limitations. A particular reference that teaches one specific non-canonical zinc finger protein identified during a search, certainly does not teach all of the others that are claimed, requiring further specific searches for each species and combination of limitations. It would be burdensome to search for each of the different species set forth, including all of

the different claim limitations drawn to different species types. As it was, because of how the elected invention was claimed, the search for the claimed invention and species far exceeded the normal time given for searching. It would be extremely burdensome to search all of the nonelected species. It is noted that the applicant has the option set forth on page 5, second full paragraph of the Office communication mailed 7/1/04 if this is the argument that the applicant is actually making concerning the election of species requirement.

7. Applicant indicates that 35 USC 121 does not require provisional species election; it requires election in response to the restriction requirement. This argument is not persuasive because election of species is a part of the restriction requirement. This requirement is taken straight from the MPEP using the long-established form paragraph that the Office requires the examiner to use.

8. Applicant, in the response filed 11/18/04 also argues that it would not be unduly burdensome to search the range of amino acid residues presented in the consensus sequence instead of just one sequence in the sequence ranges. This argument is not persuasive because it frankly was somewhat burdensome to search even just one sequence in the range because the consensus sequence is so short and non-specific that there were too many

search "hits" to review them all. The USPTO library which conducts the actual sequence search had to take special measures to reduce the number of hits to a manageable and meaningful result. The vast majority of hits were of questionable use because they identified sequences which were simply present in the genome or elsewhere without any regard as to whether they are actually zinc fingers. Searching the other sequences within the range would have made the search that much more unmanageable and thus it would have been an undue burden.

Claims 1, 3, 5, 7-9, 11-21, 23-24, 33-35, 38, and 42-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species and/or invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/3/04 and 11/18/04.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 28, 36, 37, and 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 39, etc, there is no clear positive antecedent basis for "a zinc finger binding protein according to claim 30" because claim 30 is directed to an isolated polynucleotide, not a zinc finger binding protein.

Regarding claim 10, there is no clear positive antecedent basis for "the zinc finger component" because the plural form "components" is recited in the referenced claim.

Regarding claim 28, there is no clear positive antecedent basis for "the third finger component".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2, 4, 6, 22, 25, 27, 30-32, 36, and 39-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Miesfeld et al as evidenced by Hard et al. and Schena et al.

Miesfeld et al teach an isolated polynucleotide encoding a non-naturally-occurring zinc-finger binding protein (polynucleotides, that encode mutants of the rat glucocorticoid receptor, such as the delta 70-130 mutant) (abstract; page 423, Figures 1-2 and throughout the reference) in an expression vector which is transformed into a cell for expression of the protein. The encoded protein comprises one or more non-C2H2 zinc finger components (such as the hormone binding component which is a functional domain and the non-DNA binding domain components shown in Figure 1). The mutant protein reads on a protein designed to bind to a target sequence because the mutant protein was designed to have the DNA binding domain which binds to a particular sequence. The target sequence for the mutant protein is the DNA sequence for glucocorticoid receptor, the glucocorticoid response element (GRE) (first column of page 423). The glucocorticoid receptor part of the fusion protein comprises a zinc finger of the X(3)-Cys-X(2)-(4)-Cys-X(12)-Z-X(1)-(7)-Z-X(4) type, as evidenced by Figure 1 of Hard et al which shows the rat glucocorticoid receptor sequence which

comprises X(3)-Cys-X(2)-Cys-X(12)-Lys-X(1)-Cys-X(4). The target sequence can be put into plant cells at the site of the promoter such as mentioned and evidenced in Schena et al (abstract) and thus reads on the target sequence being in a plant cell or is a promoter sequence. In the art, promoter sequences read on the whole region immediately upstream of the transcriptional start site which regulates transcription, so the target sequence of the zinc finger protein encoded by the claimed polynucleotide reads on having the target sequence be a promoter sequence. The target sequence comprises about 9 to about 14 contiguous base pairs because 26 base pairs of the GRE sequence as taught and evidenced in Schena et al (Figure 3) comprise from 1 to 26 base pairs. The mutant protein encoded by the polynucleotides taught by the reference comprise an activation domain (abstract).

Hard et al and Schena et al are only cited as evidence that the teachings of Miesfeld et al inherently meet the claim limitations as shown by the cited teachings described above.

Claims 2, 4, 6, 10, 25-27, 30-32, 36, and 39-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Lecka-Czernik (US Patent No. 5,905,146).

Lecka-Czernik teaches an isolated polynucleotide encoding a non-naturally-occurring zinc-finger binding protein (a S1-3

fusion protein comprising the three zinc fingers and the activation domain in an expression vector (pET30) in E. coli)(column 23). The encoded protein comprises one or more non-C2H2 zinc finger components (such as the activation domain which is a functional domain and the non-DNA binding domain components. The fusion protein reads on a protein designed to bind to a target sequence because the fusion protein was designed to have the DNA binding domain which binds to a particular sequence. The target sequence (which must comprise at least 9 nucleotides corresponding to the binding site of 3 nucleotides per zinc finger) for the fusion protein is found in many origins of DNA replication and overlaps a number of defined DNA binding sites for major transcription factors (i.e., in the promoter region) that have established function in cell proliferation and differentiation (and thus may be a regulator of transcriptional activity of other transcription factors) (column 4). The middle zinc finger (starting with Pro) of the protein comprises X(3)-Cys-X(2)-Cys-X(12)-His-X(3)-Z-X(4) (Figure 3B), which reads on the elected species of zinc finger component.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 4, 6, 26-28, 30-32, 36-37, and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pomerantz et al (US Patent No. 6,326,166 B1) in view of Hard et al.

Pomerantz et al teach a chimeric protein (comprising at least three zinc fingers) which comprises a composite DNA-binding region containing a zinc finger-steroid receptor fusion which comprises fingers 1 and 2 of Zif268 and the DNA-binding domains of the glucocorticoid receptor, joined at the carboxyl-terminal region of finger 2 and the amino-terminal region of the DNA-binding domain of the glucocorticoid receptor (column 2). The chimeric protein reads on a protein designed to bind to a target sequence because the chimeric protein was designed to have the DNA binding domain which binds to a particular sequence. The target sequence for the mutant protein comprises the DNA sequence for glucocorticoid receptor, the glucocorticoid response element (GRE) (first column of page 423). The target sequence comprises about 9 to about 14 contiguous base pairs because 26 base pairs of the GRE sequence (which is a part of the target sequence) comprise from 1 to 26 base pairs (as shown in the first rejection under 102(b) above. Pomerantz et al also teach the isolated DNA sequences encoding the chimeric proteins, which can be in an expression construct in a cell (column 5). It is taught that the chimeric protein may further comprise an activation domain, such as various activation domains known in the art teaching VP16 and p65 activation domains as specific examples (columns 4 and 5).

Pomerantz et al do not specifically teach the sequence of the DNA-binding domain of a glucocorticoid receptor to be used, such as the DNA-binding domain from the rat glucocorticoid receptor.

Hard et al teach the DNA-binding domain of the rat glucocorticoid receptor (Figure 1) which comprises two C4 zinc fingers both of which are non-canonical (non-C2H2) zinc fingers.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the DNA binding domain of the rat glucocorticoid receptor in an isolated polynucleotide encoding a chimeric protein comprising fingers 1 and 2 of Zif268 and the DNA-binding domain of the glucocorticoid receptor taught by Pomerantz et al because Pomerantz et al teach that it is within the ordinary skill in the art to make such a chimeric protein and Hard et al teach the sequence of a DNA-binding domain of a rat glucocorticoid receptor. It would have been further obvious to make the isolated polynucleotide encoding the chimeric protein comprising an activation domain such as VP16, place it into an expression vector, and transform cells with the polynucleotide in order to overexpress the chimeric protein, which is what Pomerantz et al teaches is within the ordinary skill in the art as the method to express the chimeric protein.

One would have been motivated to do so for the expected benefit of making a specific chimeric protein comprising the glucocorticoid receptor as suggested by Pomerantz et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 2, 4, 6, 25-28, 30-32, 36-37, and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pomerantz et al and Hard et al as applied to claims 2, 4, 6, 26-28, 30-32, 36-37, and 39-41 above, and further in view of Goff et al (US Patent No. 5,880,333).

The teachings of Pomerantz et al and Hard et al are applied as above and repeated as before.

These references do not specifically teach the use of the maize C1 activation domain (the elected species) in the chimeric protein encoded by the polynucleotide.

Goff et al teach that transactivation domains which have been shown to be particularly effective in the method of the present invention (controlling gene expression in plants) include C1 (isolated from maize) (column 10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the C1 activation domain from maize as the activation domain in the chimeric protein encoded by the polynucleotide made obvious from the teachings of Pomerantz et al and Hard et al because Pomerantz et al teach that it is within the ordinary skill in the art to use any activation domain known in the art in the chimeric protein and Goff et al teach the C1 activation domain from maize.

One would have been motivated to do so for the expected benefit of making a chimeric protein which is particularly effective at regulating expression in plant cells, as suggested by Goff et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December

28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

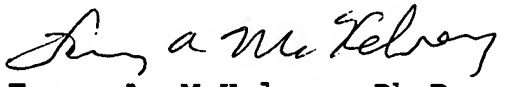
Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all

patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (571) 272-0775. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.



Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

February 7, 2005